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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/577,008	SUZUKI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/25/6,6/14/6;2/27/7;8/2/7*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on April 17, 2008 is acknowledged. The traversal is on the ground(s) that "[t]he claims of at least Groups IV and VII should be rejoined and examined in the present application. With regard to the invention of Group VII, Applicants respectfully note that if the protein of Group I is found to be novel and unobvious, i.e. the protein has never before been identified or isolated, antibodies against the protein, which require the protein for production, must also be novel and unobvious" (p. 2 of the Response). Applicant's arguments have been fully considered and found to be persuasive in part. The methods of Group IV have been rejoined. However, the invention of Group VII is considered independent and distinct for the reasons that follow.

The polypeptides of Group I and the antibodies of Group VII are patentably distinct because while the inventions of both Groups I and VII are polypeptides, in this instance, the polypeptides of Group I are single chain molecules of a secreted protein, whereas the polypeptide of Group VII encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 complementary determining regions (CDRs) that function to bind an epitope. Thus, the polypeptides of Group I and the antibodies of Group VII are structurally distinct molecules; any relationship between a polypeptide of Group I and an antibody of Group VII is dependent upon the correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies that would be generated upon immunization with a polypeptide.

In this case, the polypeptides of Group I are structurally unrelated large molecules which contain potentially hundreds of regions to which an antibody can bind, whereas the antibody of Group VII is defined in terms of its binding specificity to a small structure within the disclosed SEQ ID NO. Thus, immunization with the polypeptide of Group I would result in the production of antibodies outside the scope of Group VII. Therefore, contrary to Applicant's statement, if the protein is novel, the antibody that binds to it could be known and/or obvious because the novelty of an antibody is determined based on the novelty of an epitope of a polypeptide of Group I. Therefore, the invention of Group VII does not read on the special technical feature of the invention of Group I.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 14-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 17, 2008.

3. Claims 1-13, in so far as they are directed to Alcadein α, are under examination in the instant office action.

Claim Objections

4. Claims 1-13 are objected to for reciting non-elected subject matter (molecular embodiments of Alcadein β and γ. Appropriate correction is required.

5. Claims 1-5 are objected to because of the apparent typo or misspelling recited therein, "regionand", "regionto" and "regionis", respectively.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-6 fail to include any limitations which would distinguish the claimed proteins, peptides and compositions from those which occur in nature. In the absence of the hand of man, naturally occurring products are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). Specifically, claims 1-6, as written, do not sufficiently distinguish over Alcadein α peptides that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. Currently, the peptides recited in the claims 1-6 encompass naturally occurring fragments of the larger molecule that are produced in nature by the enzymatic processing by presenilins (see claim 3, for example).

The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by the specification. Applicant should point to the basis in the specification for any amendment to the claims. See MPEP 2105.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 1, 4 and 5 are vague and indefinite in so far as it employs the term "Alcadein α" as a limitation. This term is appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "Alcadein α". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "Alcadein α", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. Furthermore, in the instant case, claims 4-6 refer to the amino acid sequences of SEQ ID NOS: 1 and 4-12 and the relationship between Alcadein α and these identified sequences is not obvious from the claims.

11. Applicant is advised that claims 1-6 are vague and ambiguous because they encompass molecular embodiments, the structure of which cannot be clearly delineated. The claims recite references to potential cites of cleaving "Alcadein α", portions of the extracellular domains and enzymes that cleave Alcadein α, and such language absent an explicit reference to the molecular structure renders the claims vague and indefinite. Furthermore, because the structure of the claimed products is not obvious from the claims, it is impossible to evaluate if the claimed subject matter reads on specific peptides or encompasses a genus of products and if

such meets the requirements of 35 U.S.C. 112, first paragraph, written description. The proper dependency of the claims 2-6 cannot be assessed as well.

12. Claims 7-12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that delineate as what is encompassed by "a process of detecting [...] the peptide" and the final step that stands for achieving the goal recited in the preamble of the claims, such as what result means diagnosis of Alzheimer's disease (AD).

13. Claims 7 and 10 are further vague and ambiguous for recitation of "an animal". Briefly, the relationship between diagnosis of AD and "an animal" is not obvious because Alzheimer's disease is known as an exclusively human disease. Also, is the AD diagnosed in the "animal" that the peptide is detected in the body fluid taken from that animal or in a different individual? Clarification is required.

14. Claim 13 recites the limitation "molecular species of the secreted peptide" in claim 1. There is insufficient antecedent basis for this limitation in the claim. Also, the claim recites the limitation "change", which is a relative term for which no point of reference is provided within the claim.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 7-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of diagnosis of Alzheimer's disease (AD) by detecting specific fragments of Alcadein α in brain tissue of a patient, does not reasonably provide enablement for collecting data or diagnosing AD by using any other sample taken from a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 7-12 encompass methods collecting data for diagnosis of AD and for diagnosing AD by detecting the fragments of Alcadein α in body fluid or tissue taken from an animal. However, the instant specification fails to present guidance for one skilled in the art as how to use the claimed peptides in the methods of diagnosis of AD except when practiced with brain tissue samples obtained from AD patients. There is no guidance for methods of collecting data, diagnosis of AD, or working examples, which would show that the claimed methods were successfully practiced in any body fluid or any other tissue "taken from an animal", as currently written.

Claim 13 is directed to a method for screening a therapeutic agent for Alzheimer's disease and the instant specification provides no guidance, working examples, prophetic or actual ones of any therapeutic agents being successfully screened, and no explanation or scientific

rationalization as why an agent that changes the amount of secreted Alcadein α fragment can be reasonably expected to be useful in treatment of AD. It would require a significant amount of undue experimentation on part of one skilled in the art to discover how to practice Applicant's inventions, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention is the demonstration that Alcadein α is extracellularly secreted in the same manner as Aβ, the major pathological component of amyloid plaques associated with Alzheimer's disease (p. 3 of the instant specification). The specification states that the discovery of the instant invention is the new finding that Alcadein α is cleaved by the same enzyme as APP, the precursor molecule of Aβ (p. 3). It is further stated that the fragments of Alcadein α, which are generated by the enzymatic processing of Alcadein α "cleaving at N-terminal and C-terminal regions [can be used as] a diagnostic marker for Alzheimer's disease" (p. 8-9). The working examples at pp. 23-29 show that in brain tissue of mice, APP and Alcadein α are colocalized (Example 1) and that Alcadein α and APP are detected in brain tissue of AD patients (Examples 2 and 3). The Examples at pp. 30-55 describe results of the experiments performed on transfected cells to study processing of Alcadein α and resulting cleavage products of Alcadein α.

With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification (see MPEP 2111 [R-1], which states that claims must be given their broadest reasonable interpretation

"During patent examination, the pending claims must be "given *>their< broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

As such, the broadest reasonable interpretation of the methods of claims 6-12 is that it allows the diagnosis of AD by detecting or determining the fragments of Alcadein α in any body fluid or tissue sample. Thus, the claims encompass samples like hair, saliva, breast milk etc. As opposed to the claims, what is disclosed about the claimed method is narrow: a single set of examples obtained on post-mortem brain tissue staining of samples taken from AD patients and no other obvious specific examples of any other samples or guidance as how to practice the full scope of instant claimed method using other types of sample.

While the skill level in the art is high, the level of predictability is low. The instant specification fails to present any factual evidence or a line of sound scientific reasoning to support a conclusion that the limited data obtained on brain tissue samples stained with anti-

Alcadein α antibody can be directly extrapolated to using any sample obtained from a subject suspected of AD and stained in the similar manner to diagnose Alzheimer's disease. Therefore, in order to practice the full scope of the instant claimed methods, a skilled practitioner would have to engage in the significant experimentation to research and discover what other samples contain Alcadein α in measurable amounts and which of these samples display the pattern that allows a differential diagnosis of AD.

With respect to claim 13, which encompasses screening for therapeutic agents to treat AD by measuring the change in secretion of Alcadein α fragments, the instant specification provides no explanation in the form of scientific reasoning, description of repeatable experiments, sound data or reference to prior art, as why a process of secretion of Alcadein α is relevant to the etiology of AD. The specification provides little evidence linking the processing of Alcadein α with the processing of APP. One skilled in the art would be required to perform significant further research on the instant claimed method in order to identify a specific biological activity of Alcadein α, its significance to AD pathology and, further, what change, if any, in the amount of Alcadein α would be beneficial for clinical purposes. For example, if a test compound was identified by the claimed method as being capable to increase the amount of Alcadein α, what would that mean to the skilled artisan? Is it a potential drug, or would administering the compound be likely to acerbate the disease? Thus, the specification provides inadequate evidence to show that a compound that changes the secretion of Alcadein α would be useful in treating AD.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. If mere plausibility were the test

for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

Conclusion

17. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

June 30, 2008

/Olga N. Chernyshev, Ph.D./
Primary Examiner, Art Unit 1649